

CORRELATION BETWEEN CAPNOGRAPHY AND ARTERIAL CARBON DIOXIDE BEFORE, DURING, AND AFTER SEVERE CHEST INJURY IN SWINE

Claire Larson Isbell, Andriy I. Batchinsky, Katherine M. Hetz,
William L. Baker, and Leopoldo C. Cancio

US Army Institute of Surgical Research, Fort Sam Houston, Texas

Received 22 Jun 2011; first review completed 11 Jul 2011; accepted in final form 16 Sep 2011

ABSTRACT The relationship between end-tidal carbon dioxide (EtCO₂) and arterial carbon dioxide (PaCO₂) if better defined could facilitate the difficult task of ventilation in prehospital trauma patients. We aimed to study the PaCO₂-EtCO₂ relationship before, during, and after chest trauma, hemorrhage, and resuscitation in swine. Twenty-four swine were intubated, anesthetized, and monitored in an animal intensive care unit during three phases: phase 1 (day 1, healthy animals); phase 2 (day 2, injury), which consisted of blunt chest trauma, hemorrhage, and resuscitation; and phase 3 (day 2, after injury). “Respiratory maneuvers” (changes in respiratory rate and tidal volume [TV], intended to vary the PaCO₂ over a range of 25 to 85 mmHg, were performed during phases 1 and 3. End-tidal CO₂ and PaCO₂ were recorded after each respiratory maneuver and analyzed using linear regression. During phase 1, PaCO₂ and EtCO₂ were strongly correlated ($r^2 = 0.97, P < 0.01$). During phase 2, animals developed decreased oxygenation (PaO₂:FiO₂ [fraction of inspired oxygen] ratio <200) and hypotension (mean arterial pressure, 20–50 mmHg); the PaCO₂-EtCO₂ relationship deteriorated ($r^2 = 0.25, P < 0.0001$). During phase 3, oxygenation, hemodynamics, and the PaCO₂-EtCO₂ relationship recovered ($r^2 = 0.92, P < 0.01$). End-tidal CO₂ closely correlates to PaCO₂ in healthy animals and after injury/resuscitation across a wide range of respiratory rates and tidal volumes. Once oxygenation and hemodynamics are restored, EtCO₂ can be used to predict PaCO₂ following chest trauma/hemorrhage and should be considered for patient monitoring. This work demonstrated that EtCO₂ alone can reliably be used to estimate PaCO₂ in uninjured subjects and in those subjects who have been resuscitated from severe injury. Immediately after blunt chest injury, the correlation between EtCO₂ and PaCO₂ is temporarily unstable. Under these circumstances (with abnormal oxygenation and/or hemodynamics), greater caution and other monitoring tools may be required.

KEYWORDS End-tidal carbon dioxide, pulmonary contusion, pulmonary dead space, swine, blood gas analysis, carbon dioxide

INTRODUCTION

After experiencing severe trauma, patients may require advanced airway control for respiratory support before reaching the hospital. In a large retrospective study ($n = 9,018$) concerning prehospital transport of trauma patients, endotracheal intubation occurred in the field 16.7% of the time (1). In addition to securing a patent airway, first responders must attempt to achieve adequate ventilation, as hyperventilation or hypoventilation can have adverse effects on the patient’s acid-base status. Davis and colleagues (2) showed a higher mortality in head-injured patients who were hyperventilated or hypoventilated ($n = 890$ intubated and $n = 2,709$ nonintubated) before hospital arrival. Adverse effects of ventilation are especially noticeable in the setting of traumatic brain injury (TBI); hyperventilation can worsen outcomes by reducing intracranial blood flow and parenchymal perfusion, whereas hypoventila-

tion causes decreased oxygen delivery (3, 4). Additional risks associated with hyperventilation include overinflation of airspaces and potential worsening of airway injury by barotrauma. Overinflation could also worsen a tension pneumothorax and lead to cardiovascular collapse. In the setting of cardiac arrest, hyperventilation can worsen coronary perfusion by increasing intrathoracic pressure (5). These scenarios highlight the need for normoventilation and normocapnia during prehospital transport of trauma patients to decrease mortality and improve outcomes.

The criterion standard by which to assess arterial carbon dioxide (PaCO₂) levels is to perform arterial blood gas (ABG) analysis. However, in the early stages of trauma casualty extraction and transport (prehospital), ABG analysis is not feasible (6). Capnography has emerged as a noninvasive surrogate for PaCO₂. Use of continuous capnography with adaptive ventilation strategies in the prehospital setting has shown improvement in achieving normocapnia in trauma patients (7). Helm and colleagues (7) compared anesthetist delivery of prehospital ventilation either using continuous capnography versus no capnography. Patients with head and chest trauma, hemodynamic instability, or a higher injury severity score arrived more frequently in the normocapnic range when ventilation was guided using capnography compared with using no capnography monitor. In light of these findings, capnography represents a potential method by which to improve ventilation during the prehospital phase of care in trauma victims.

The correlation between end-tidal CO₂ (EtCO₂) and PaCO₂ is well known, and a PaCO₂-EtCO₂ gradient (defined as PaCO₂ – EtCO₂) of 5 to 10 mmHg is expected in an otherwise healthy patient. This gradient is a function of pulmonary dead space and

Address reprint requests to Leopoldo C. Cancio, MD, COL, MC, US Army, 3698 Chambers Pass, Ft Sam Houston, TX 78234. E-mail: Lee.cancio@us.army.mil.

This study was funded by the Combat Casualty Care Research Program (Combat Critical Care Engineering Task Area), US Army Institute of Surgical Research, and US Army Medical Research and Materiel Command, Ft Detrick, Maryland.

All work was performed at the US Army Institute of Surgical Research, Ft Sam Houston, Texas.

This study has been conducted in compliance with the Animal Welfare Act, the Implementing Animal Welfare Regulations, and in accordance with the principles of the Guide for the Care and Use of Laboratory Animals.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

DOI: 10.1097/SHK.0b013e3182391862

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Report Documentation Page

*Form Approved
OMB No. 0704-0188*

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1. REPORT DATE 01 JAN 2012	2. REPORT TYPE N/A	3. DATES COVERED -			
4. TITLE AND SUBTITLE Correlation between capnography and arterial carbon dioxide before, during, and after severe chest injury in swine					
6. AUTHOR(S) Isbell C. L., Batchinsky A. I., Hetz K. M., Baker W. L., Cancio L. C.,					
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX					
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)					
10. SPONSOR/MONITOR'S ACRONYM(S)					
11. SPONSOR/MONITOR'S REPORT NUMBER(S)					
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release, distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF: <div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;"> a REPORT unclassified </div> <div style="text-align: center;"> b ABSTRACT unclassified </div> <div style="text-align: center;"> c THIS PAGE unclassified </div> </div>			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 7	19a. NAME OF RESPONSIBLE PERSON

cardiac output (CO) and has been shown to change in pathologic conditions that affect these physiologic variables (8). Pulmonary contusion (PC) is a common injury endured as a result of trauma that may decrease CO and increase dead space (9, 10). No studies to date have described the effect of PC on the gradient. We sought to describe and model the relationship between EtCO_2 and PaCO_2 in the setting of PC with hemorrhage and resuscitation in swine. We hypothesized (*a*) that, before injury, the relationship between EtCO_2 and PaCO_2 would be linear and the gradient would be low and (*b*) that, after injury, the relationship would lose linearity and the gradient would increase.

MATERIALS AND METHODS

This study was approved by the US Army Institute of Surgical Research Animal Care and Use Committee and was carried out in accordance with the guidelines set forth by the Animal Welfare Act and other federal statutes and regulations relating to animals and studies involving animals.

Animal preparation and measurements

Female Yorkshire pigs (Midwest Research Swine, Gibbon, Minn) ($n = 24$) weighing 30 to 45 kg were fasted overnight and premedicated with glycopyrrolate. Anesthesia was induced using inhaled isoflurane (0.5–3 vol %). Animals were intubated, and total intravenous anesthesia (TIVA) using initial rates of midazolam (25 mg/h), ketamine (250 $\mu\text{g}/\text{kg}/\text{min}$), and propofol (150 $\mu\text{g}/\text{kg}$ per min as needed) was administered through an ear vein. Isoflurane was then discontinued. Total intravenous anesthesia was titrated during all procedures to achieve no response to painful stimuli. A Foley catheter was placed into each animal's urethra with the use of a speculum. The following procedures were then performed: tracheostomy, bilateral femoral artery and vein catheter placement, and right external jugular catheter placement. The animal was in the supine position for the duration of surgical preparatory procedures. After surgical preparation, the animals were placed in sternal recumbent position in the animal intensive care unit (ICU) and mechanically ventilated using a Draeger EVITA XL ventilator (Draeger Medical, Telford, Pa) in controlled mechanical ventilation mode with a tidal volume (TV) of 10 mL/kg and a respiratory rate (RR) of 12 breaths/min. The RR was then adjusted as necessary to achieve a normal arterial carbon dioxide level (35–45 mmHg) per i STAT (Abbott Laboratories, Abbott Park, Ill) ABG analysis. Fraction of inspired oxygen (Fio_2) was set to 21%; positive end expiratory pressure was set to 5 mmHg. A pulmonary arterial catheter was inserted through the right external jugular vein and provided core temperature, central venous pressure (CVP, in millimeters of mercury), and continuous CO (in liters per minute) (Vigilance II; Edwards Lifesciences, Irvine, Calif). A capnograph (COSMO; Philips Respironics, Amsterdam, the Netherlands) was connected at the endotracheal tube and used to measure EtCO_2 .

The variables measured during this experiment were as follows: time (in minutes), Fio_2 (in percentage), TV (in milliliters per kilogram), pulse oximetry (SpO_2), RR (in breaths per minute), heart rate (in beats per minute), mean arterial pressure (MAP, in millimeters of mercury), EtCO_2 (in millimeters of mercury), ABG, and ratio of arterial oxygen content (PaO_2) to Fio_2 (PFR). All data collection was during three phases (1, 2, and 3) of the experiment conducted in an ICU environment. The SpO_2 monitor (Oxisensor II 1.20; Covidien; Nellcor, Mansfield, Mass) was placed on the tail; Fio_2 was titrated based on the SpO_2 reading by the following method: If SpO_2 was less than 90%, the Fio_2 was increased by 5% every 1 to 2 min until SpO_2 was 90% or greater. If SpO_2 was greater than 90% and Fio_2 was greater than 21%, Fio_2 was decreased by 5% every 1 to 2 min until either SpO_2 of 90% or greater or Fio_2 was 21%, whichever event came first.

The experiment was completed over three phases, with overnight ICU monitoring and sedation between phases 1 and 2. On day 1, animals underwent surgical preparation. Then, they underwent respiratory maneuvers in the uninjured state (phase 1; see below). Animals were then allowed to rest overnight. The animals were cared for by a veterinary technician overnight with a physician on call for clinical support. On day 2, animals underwent an injury sequence (phase 2) including PC, hemorrhage, shock period (30 min), and resuscitation. The specifics of this sequence are detailed below. Following the injury sequence, the respiratory maneuvers were again performed (phase 3) in the same order as before. Each animal received approximately 5 min of inhaled isoflurane at the start of instrumentation and approximately 27 h of TIVA before experiment end. After completion of phase 3, animals were killed using a high dose of sodium pentobarbital (Fatal Plus, Dearborn, Mich).

Experimental protocol: respiratory maneuvers (phases 1 and 3)

We performed a sequence of ventilator changes across a wide range of minute ventilations by altering either RR or TV to hyperventilate or hypoventilate the animal. We termed these changes "respiratory maneuvers," and we completed them during both the uninjured (day 1, phase 1) and injured states (day 2, phase 3) in all animals. After baseline measurements, each animal was randomized to one of four groups to determine the sequence by which the animal would undergo the respiratory maneuvers. These groups are listed in Table 1. All animals went through every ventilator change, but because of randomization, the sequence of respiratory maneuvers differed among animals. Before respiratory maneuvers, animals were determined to have adequate anesthesia without response to painful stimuli. Animals were then administered boluses of vecuronium (1 mg/kg) to ensure absence of spontaneous respirations during the maneuvers. Two sets of data were collected, and the results averaged after each respiratory maneuver.

Experimental protocol: phase 2

All animals underwent injury on day 2. Injury consisted of right sided PC delivered as previously described using a modified captive bolt humane stunner (model MKL, Karl Schermer; Packers Engineering, Omaha, Neb) (10). Immediately after PC, a chest tube was placed on the side of impact. Ten minutes after PC, constant rate hemorrhage was performed, for a total volume of 12 mL/kg over 10 min. The blood was removed through an arterial line and stored in citrated blood collection bags (Terumo, Somerset, NJ). The animal was observed for 30 min following the end of hemorrhage. Then, a pressure bag was used to administer warm lactated Ringer's (LR) solution at a volume of three times the volume of shed blood over a 10 min period. After administration of LR solution, the animals were transfused with the previously collected blood. Administration of LR solution was then started at a rate of two times the body weight per hour and titrated to achieve a urine output of at least 1 mL/kg per hour. It should be noted that no respiratory maneuvers were performed during this phase. The animals were then returned to the sternal recumbent position, and respiratory maneuvers were again performed as described above.

Statistical analysis

All data are means ($\pm\text{SEM}$) of MAP, PFR, EtCO_2 , or PaCO_2 at each respiratory maneuver during phases 1 and 2 and were analyzed for statistical differences using a Wilcoxon signed rank test. Phase 2 data were recorded over time, and a two way analysis of variance with repeated measures was performed on EtCO_2 and PaCO_2 to determine if time from injury had any impact on the relationship between them. Variables suspected to play a role in predicting PaCO_2 were MAP, PFR, and EtCO_2 . We used those variables in step wise linear regression to model the relationship between EtCO_2 and PaCO_2 during phases 1, 2, and 3. All statistics were completed using Stata (StataCorp, College Station, Tex) or SAS (SAS Institute Inc, Cary, NC) software.

RESULTS

Twenty-four animals underwent experimental procedures. More than 700 h of animal ICU care were used to complete this protocol. Four animals died after phase 1, of whom two died immediately following PC as a direct result of the impact. Necropsy revealed massive pulmonary parenchymal and vascular injury, which was deemed to be the cause of death. The other two animals died on day 1 from spontaneous dysrhythmias attributed to the indwelling pulmonary artery catheter. Each animal developed ventricular tachycardia and subsequent pulseless electrical activity. Necropsy revealed small clots and endocardial irritation within the right atrium with evidence of trauma due to the pulmonary artery catheter. Cardiac irritation was deemed to be the cause for the fatal dysrhythmias and hence death. For the final analysis, all 24 animals were used to examine phase 1 data, and the 20 animals surviving to the end of study were used to examine phase 3 data. Data were recorded continuously during phase 2 for 13 animals and constitute the subset of animals used for phase 2 analysis.

TABLE 1. Order by which animals underwent ventilator changes

Group no.: No. animals in each group	Description of sequence of respiratory maneuvers RR, TV	Example
Group 1: eight animals	Each ventilator change is separated by seven min: 1. Increase RR by 2/min to maximum of 30/min 2. Change RR back to baseline settings and increase TV to 20 mL/kg 3. Decrease TV by 2 mL/kg until 4 mL/kg is reached 4. Change TV back to 10 mL/kg and decrease RR to 6/min 5. Increase RR by 2/min until baseline setting is reached	Start: TV = 10 mL/kg, RR = 14 1. TV hold at 10 mL/kg: increase RR = 16, = 18, = 20, ..., RR = 30 2. Change RR = 14, TV = 20 mL/kg 3. RR hold at 14: decrease TV = 20 mL/kg, = 18 mL/kg, = 16 mL/kg, ..., = 4 mL/kg 4. Change TV = 10 mL/kg, RR = 6 5. TV hold at 10 mL/kg: increase RR = 6, = 8, = 10, = 12, = 14 End
Group 2: five animals	Each ventilator change is separated by seven min: 1. Increase TV by 2 mL/kg until a maximum of 20 mL/kg is reached 2. Change TV back to 10 mL/kg and increase RR to 30/min 3. Decrease RR by 2/min until 6/min is reached 4. Change RR back to baseline settings and decrease TV to 4 mL/kg 5. Increase TV by 2 mL/kg until 10 mL/kg is reached	Start: TV = 10 mL/kg, RR = 14 1. RR hold at 14/min: Increase TV to = 12 mL/kg, = 14 mL/kg, ..., = 20 mL/kg 2. Change TV = 10 mL/kg, RR = 30 3. TV hold at 10 mL/kg, decrease RR = 30, = 28, = 26, ..., = 6 4. Change RR = 14, TV = 4 mL/kg 5. RR hold at 14, increase TV = 4 mL/kg, = 6 mL/kg, ..., = 10 mL/kg End
Group 3: six animals	Each ventilator change is separated by 7 min 1. Decrease RR by 2/min to a minimum of 6/min 2. Change RR back to baseline settings and decrease TV to 4 mL/kg 3. Increase TV by 2 mL/kg until 20 mL/kg is reached 4. Change TV back to 10 mL/kg and increase RR to 30/min 5. Decrease RR by 2/min until baseline setting is reached	Start: TV = 10 mL/kg, RR = 14 1. TV hold at 10 mL/kg: decrease RR = 14, = 12, ..., = 6 2. Change TV to 4 mL/kg, RR = 14 3. RR hold at 14: increase TV = 4 mL/kg, = 6 mL/kg, = 8 mL/kg, ..., = 20 mL/kg 4. Change TV = 10 mL/kg, RR = 30 5. TV hold at 10 mL/kg: decrease RR = 30, = 28, = 26, ..., = 6 End
Group 4: five animals	Each ventilator change is separated by 7 min 1. Decrease TV by 2 mL/kg until a minimum of 4 mL/kg is reached 2. Change TV back to 10 mL/kg and decrease RR to 6/min 3. Increase RR by 2/min until 30/min is reached 4. Change RR back to baseline settings and increase TV to 20 mL/kg 5. Decrease TV by 2 mL/kg until 10 mL/kg is reached	Start: TV = 10 mL/kg, RR = 14 1. RR hold at 14/min: Decrease TV to = 8 mL/kg, = 6 mL/kg, ... 4 mL/kg 2. Change TV = 10 mL/kg, RR = 6 3. TV hold at 10 mL/kg, increase RR = 6, = 8, = 10, ..., = 30 4. Change RR = 14, TV = 20 mL/kg 5. RR hold at 14, decrease TV = 18 mL/kg, = 16 mL/kg, ..., = 10 mL/kg End

Note that although animals underwent changes in different orders, they all rotated through every possible ventilator change.

Phase 1

Multivariate stepwise linear regression to model PaCO₂ was done using the following variables: MAP, PFR, and EtCO₂ in the healthy animal (phase 1). End-tidal CO₂ had the strongest association with PaCO₂. Adding MAP did not show an increase in correlation and was therefore left out of the final model. Ratio of Pao₂ to Fio₂ was not associated with PaCO₂. Using EtCO₂ alone as the independent variable and including all ventilator changes (RR and TV) on day 1, the association with PaCO₂ was strong: PaCO₂ = $-0.98 + 0.96 * \text{EtCO}_2$ ($r^2 = 0.97$, $P < 0.05$) (Fig. 1).

Phase 2

Immediately upon impact, MAP decreased dramatically. Mean arterial pressure then decreased again during the hemorrhage period (Figs. 2, 2–3) and slowly recovered during the shock period (Figs. 2, 3–4), resuscitation with LR solution (Figs. 2, 4–5), and transfusion (Figs. 2, 5–6). Ratio of Pao₂ to Fio₂ decreased markedly from baseline (Fig. 3, 0) to 10 min following impact (Figs. 2 and 3) and remained 300 or less during the entire injury/resuscitation sequence.

Figure 4 shows EtCO₂ and PaCO₂ during phase 2. Within seconds of impact, the PaCO₂ remained relatively constant,

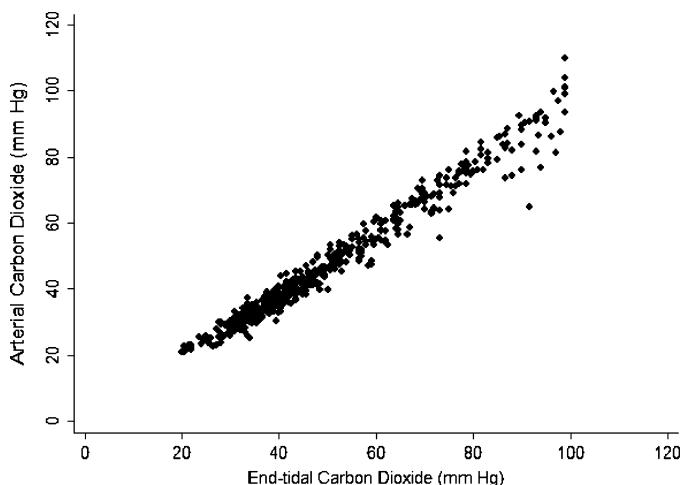


FIG. 1. Scatter plot for EtCO_2 (x axis) vs. PaCO_2 (y axis) during phase 1 (healthy animal respiratory maneuvers, day 1), $n = 24$. Equation is $\text{PaCO}_2 = 0.98 + 0.96 * \text{EtCO}_2$, $r^2 = 0.97$, $P < 0.05$.

whereas EtCO_2 decreased dramatically. Over the next 10-minute period, EtCO_2 recovered partially. No interaction was noted between the PaCO_2 - EtCO_2 gradient and time until the start of blood transfusion (Figs. 4, 5). After this time point, EtCO_2 and PaCO_2 began to converge as time progressed.

Univariate regression of EtCO_2 and PaCO_2 during phase 2 indicated a weaker association than during the other phases (1 and 3), and an increase in the gradient: $\text{PaCO}_2 = 26.8 + 0.49 * \text{EtCO}_2$ ($r^2 = 0.25$, $P < 0.0001$, $n = 13$). The relationship is illustrated in Figure 5. Mean arterial pressure and PFR were found to have a stronger association with PaCO_2 than during phases 1 or 3 and could be included in a multivariate linear regression model. Using all variables (MAP, PFR, and EtCO_2), the equation is $\text{PaCO}_2 = 23.9 + (0.52 * \text{EtCO}_2) + (-0.04 * \text{PFR}) + (0.19 * \text{MAP})$. Despite inclusion of these other variables, the association remained weaker than observed either before injury or after transfusion ($r^2 = 0.51$, $P < 0.001$).

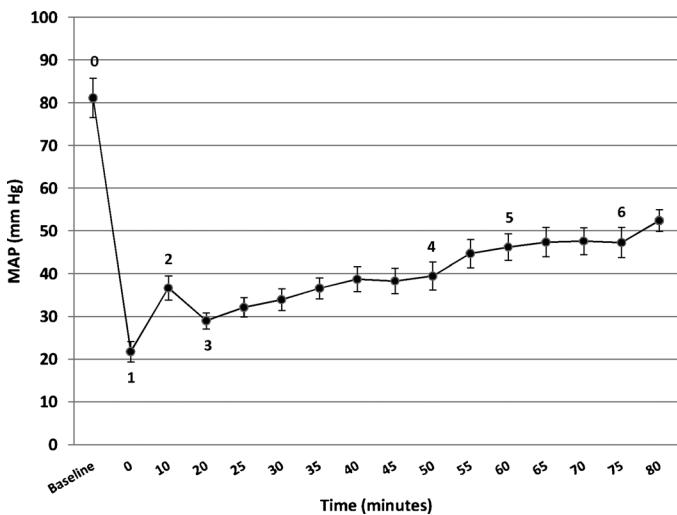


FIG. 2. Mean arterial pressure (in millimeters of mercury) during phase 2. Means ($\pm \text{SEM}$) are shown. Numbers correspond to the following events: 0. Baseline (before contusion); 1. Pulmonary contusion; 2. Start hemorrhage; 3. End hemorrhage, start shock period; 4. End shock period, start LR solution administration; 5. End LR solution administration, start autologous blood transfusion; 6. Completion of autologous blood transfusion.

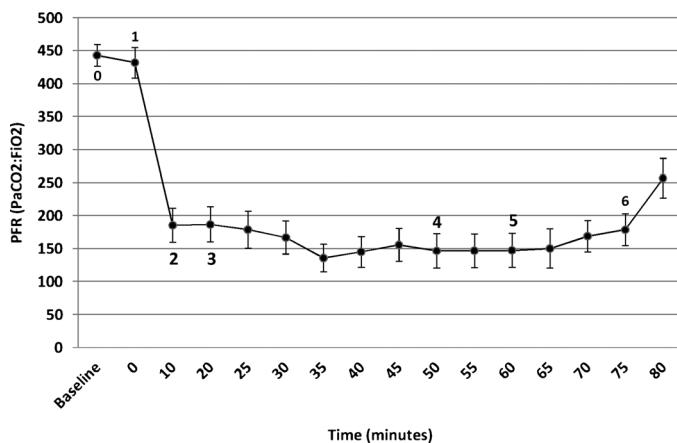


FIG. 3. Ratio of PaO_2 to Fio_2 during phase 2. Means ($\pm \text{SEM}$) are shown. Numbers correspond to the following: 0. Baseline (Before contusion); 1. Pulmonary contusion; 2. Start hemorrhage; 3. End hemorrhage, start shock period; 4. End shock period, start LR solution administration; 5. End LR solution administration, start autologous blood transfusion; 6. Completion of autologous blood transfusion.

Phase 3

Overall, MAP was lower (considering both sets of respiratory maneuvers together) during phase 3 than during phase 1 ($P < 0.0001$). Despite PC and hemorrhage, the PFR recovered to greater than 300 during phase 3. However, the PFR was higher during phase 1 compared with phase 3 ($P < 0.0001$). Hypoventilation adversely affected PFR, particularly at the lower end of TV, during both phases 1 and 3; ventilation with 4 mL/kg caused PFR of less than 300 in both injured and uninjured.

End-tidal CO_2 was statistically different (between phases 1 and 3) during changes in RR and TV ($P < 0.05$). By contrast, PaCO_2 values were not different comparing phase 1 with phase 3 during the same changes in RR and TV ($P > 0.05$). As in phase 1, higher PaCO_2 and EtCO_2 were noted during low TV ventilation compared with low RR ventilation.

During phase 3, linear regression was again performed to model the PaCO_2 - EtCO_2 relationship. The equation for this phase was $\text{PaCO}_2 = 2.52 + 0.97 * \text{EtCO}_2$ (Fig. 6). The association

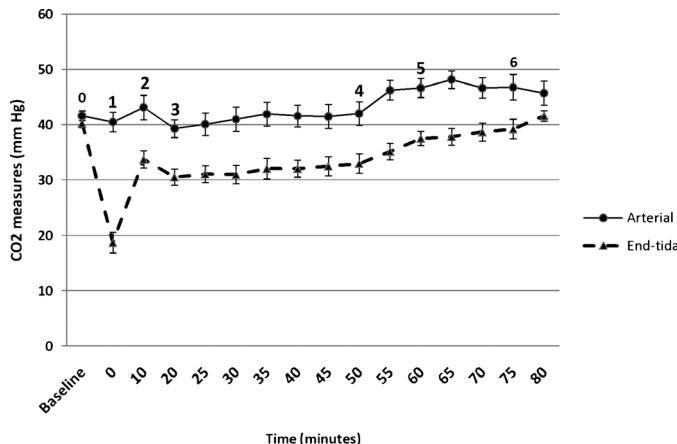


FIG. 4. CO_2 measures during phase 2, comparisons of arterial (PaCO_2) and end-tidal (EtCO_2). Means ($\pm \text{SEM}$) are shown. Numbers correspond to the following: 0. Baseline (Before contusion); 1. Pulmonary contusion; 2. Start hemorrhage; 3. End hemorrhage, start shock period; 4. End shock period, start LR solution administration; 5. End LR solution administration, start autologous blood transfusion; 6. Completion of autologous blood transfusion.

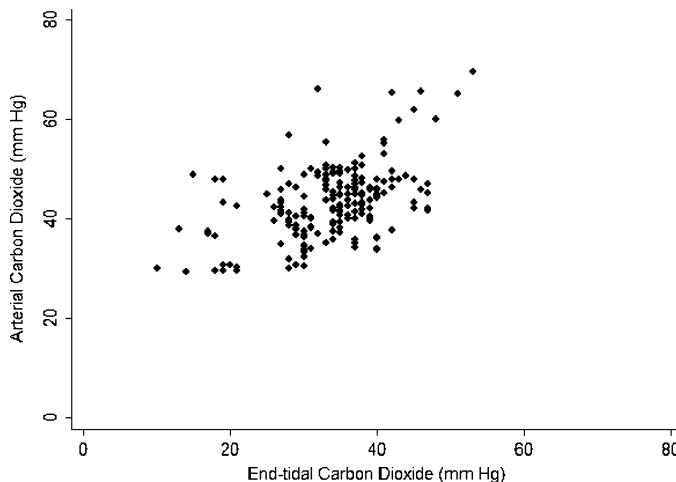


FIG. 5. Scatter plot for EtCO₂ (x axis) vs. PaCO₂ (y axis) during phase 2 (day 2), $\text{PaCO}_2 = 26.8 + 0.49 \times \text{EtCO}_2$, $r^2 = 0.25$, $P < 0.0001$, $n = 13$.

between EtCO₂ and PaCO₂ was again shown to be strong ($r^2 = 0.92$, $P < 0.05$), although slightly weaker than for phase 1 data. Ratio of Pao₂ to Fio₂ was not associated with PaCO₂, and the addition of MAP to the model did not improve it.

DISCUSSION

The principal findings in this study are as follows: (a) EtCO₂ and PaCO₂ were closely correlated in uninjured, mechanically ventilated pigs across a wide range of TVs and RRs; (b) EtCO₂ and PaCO₂ were also correlated in injured and resuscitated pigs with a difference of approximately 2.5 mmHg across a similar range of TVs and RRs; (c) EtCO₂ and PaCO₂ showed a weaker correlation during the immediate postinjury period, with a gradient of 22 mmHg.

Capnography is a vital tool in the armamentarium of aeromedical teams and first responders (11). Some health care providers who are involved in the prehospital transport of casualties are now relying on continuous EtCO₂ monitoring rather than one-time capnometry for verification of correct placement of an airway. In their prospective observational study, Silvestri et al. (12) examined patients ($n = 153$) who were intubated before facility arrival. In those whose intubation was monitored using continuous capnography (93/153), the rate of unrecognized displaced endotracheal tubes was 0%, whereas the rate for the patients without continuous monitoring (60/153) was 9%. Kober et al. (13) demonstrated capnography's utility in nonintubated trauma victims ($n = 70$) when they compared sensor malfunction rate during transport between pulse oximetry and capnography. Capnography was not found to be more inconvenient to the patients and gave disruption alerts only 0.8% of the transport time, compared with 13.2% for the pulse oximeter (13). Despite these demonstrated benefits of continuous capnography, it is currently not being fully utilized during the prehospital phase of trauma care.

Prehospital casualty retrieval and transport involve advanced airway control in a significant percentage of patients either by endotracheal intubation, bag-valve-mask, laryngeal mask airway, Combitube, or other apparatus (14, 15). Controlling CO₂

levels and ventilation adequacy during this period can improve short-term acid-base status and improve long-term outcomes in trauma patients (1, 16, 17). Arguably, TBI patients can most benefit from tight control of blood CO₂ levels so as to improve brain perfusion during the crucial 24 to 48 h after injury (18). Current recommendations from the literature include targeting PaCO₂ levels between 35 and 40 mmHg so as to achieve optimal outcomes in these situations (19–21). Several studies indicate that a sizeable number of patients with TBI reach the hospital having been inappropriately ventilated (22, 23). Hyper-ventilation and hypoventilation during this period, especially in the setting of TBI, increase mortality rates (2, 3). Dumont et al. (16) retrospectively examined 77 patients with TBI admitted to a level I trauma center over a period of 7 years (January 2000 to January 2007) to determine if PaCO₂ level on arrival was associated with in-hospital mortality. Patients with normocapnia had a lower mortality rate (15%) compared with those who were hypercapnic (61%) or hypocapnic (77%) ($P = 0.045$ between groups) (16).

The use of continuous capnography during prehospital transport has already been shown in some studies to improve ventilation adequacy (7). Davis (3) demonstrated that using continuous capnography reduces hyperventilation but does not eliminate it. However, creating a specific algorithm to achieve tight control can improve normoventilation even further. Helm and colleagues (7) have also shown that using continuous capnography during the prehospital care of trauma patients increases the likelihood that the patient will arrive at the hospital normocapnic. In their study, patients with chest trauma or hemodynamic instability were more likely to be normoventilated on hospital arrival when capnography was used to guide ventilation (7).

Our study makes use of a controlled large animal model before, during, and after isolated chest trauma, hemorrhage, and resuscitation—with time points intended to simulate injury, extraction, transport, and resuscitation. Our data demonstrate a close association between PaCO₂ and EtCO₂ during periods of hemodynamic stability in both uninjured animals and injured animals with a history of chest trauma in which adequate

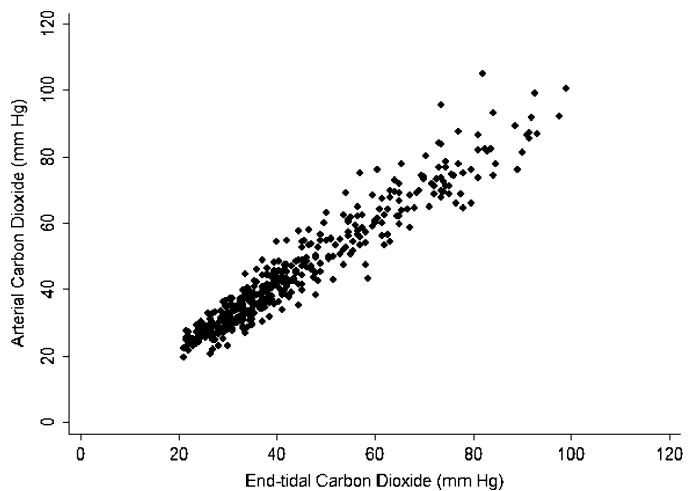


FIG. 6. Scatter plot for EtCO₂ (x axis) vs. PaCO₂ (y axis) during phase 3 (injured animal respiratory maneuvers, day 2), $n = 20$. Equation is $\text{PaCO}_2 = 2.52 + 0.97 \times \text{EtCO}_2$, $r = 0.92$, $P < 0.05$.

oxygenation (PFR >300) has been restored. Immediately after injury (during the first 90 min after PC), oxygenation (PFR) and hemodynamics (MAP) are shown to play a role in the gradient between PaCO_2 and EtCO_2 . The relationship between EtCO_2 and PaCO_2 is related to physiologic dead space, ventilation-perfusion (V/Q) matching, and CO (24, 25). This has been shown by McSwain and colleagues (8) in a retrospective cross-sectional study in which they examined pediatric ICU patients comparing PaCO_2 and EtCO_2 gradient as it relates to the ratio of physiologic dead space (V_D) to tidal volume (V_T). They showed that a strong correlation ($\rho = 0.95$) exists between the PaCO_2 - EtCO_2 relationship at low physiologic dead space ($V_D:V_T \leq 0.4$) and that the correlation remains strong ($\rho = 0.86$) to moderately strong ($\rho = 0.78$) at increasing levels of dead space ($V_D:V_T = 0.56-0.7$ and $V_D:V_T > 0.7$, respectively). The PC model used by us has been shown to lead to increased $V_D:V_T$ and thus seems to provide an appropriate setting to test the dynamics of the PaCO_2 - EtCO_2 gradient (9, 10).

The use of capnography in trauma patients has been discouraged because of some studies that showed a lack of correlation between EtCO_2 and PaCO_2 in this population. Russell and Graybeal (26) examined the correlation between EtCO_2 and PaCO_2 in nine trauma patients in an ICU setting. In 78% of patients, a significant ($P < 0.05$) relationship was found between these two variables. However, individual gradients ranged from -2 to 36 with a mean of 14 ± 11 mmHg, and the correlations were not always positive or negative. A larger gradient between these two variables was found in situations of decreasing oxygenation, an observation that we made from our data as well. Belpomme and colleagues (27) examined the gradient between EtCO_2 and PaCO_2 in the prehospital setting in both trauma and nontrauma patients, and they concluded that EtCO_2 could not be used to reliably estimate PaCO_2 . The patients in their study were quite hypoxic, however, and required on average $72\% \pm 19\%$ to $78\% \pm 20\%$ FIO_2 . The study included eight trauma patients, whereas the remaining 92 patients had a variety of other medical disorders, some with compromised lung mechanics. Both these factors would decrease the correlation between EtCO_2 and PaCO_2 as evidenced by our model during the acute injury period (phase 2).

To optimize the usefulness of continuous capnography in trauma, we must specifically define how the PaCO_2 - EtCO_2 relationship changes after different levels of injury and with regard to the area of body injured. No study has examined this gradient in patients with history of trauma, who regain hemodynamic stability after resuscitation. Our study in swine simulates such a scenario. The MAP and PFR of the animals improved greatly after administration of fluid and blood. After that point, we showed that the EtCO_2 and PaCO_2 converge, with a difference of only 2.5 mmHg. This finding leads us to believe that, after trauma, in the setting of hemodynamic stability and adequate oxygenation, using EtCO_2 as a surrogate for PaCO_2 is a viable option—especially in a situation in which ABG analysis cannot be performed.

The EtCO_2 - PaCO_2 relationship lost robustness in the period immediately following PC and then improved again to near baseline levels as oxygenation and hemodynamics recovered. To further investigate the relationship between EtCO_2 and PaCO_2

in the setting of prolonged hypoxemia, studies are underway in a bilateral chest injury model.

Our data indicate that, in healthy animals, the gradient between PaCO_2 and EtCO_2 was approximately -1 mmHg (i.e., slightly higher EtCO_2 than PaCO_2). Several potential explanations exist for a negative gradient. Rebreathing of previously exhaled air in the ventilator circuit could create a mixture of previously exhaled CO_2 and newly exhaled CO_2 . In addition, low (but finite) V/Q lung units may also decrease the gradient. Fletcher and colleagues (28) outline the physiology behind this finding and state, “the negative... gradient implies compensation by perfusion for early emptying, overventilated alveoli.”

Finally, we concede that patients most likely will not have indwelling arterial catheters in the prehospital setting. Venous blood gas analysis could also be a viable method by which to estimate a patient’s acid-base status. In our current model, we did not measure real-time concordant venous blood gases, but this practice should be further investigated in view of our current findings and explored as a potential tool by which to facilitate capnography-driven ventilation control.

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